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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/771,680	02/03/2004	Dong-Er Zhang	AP35943-074779.0105	4033

21003 7590 10/14/2005

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EXAMINER	
GRUN, JAMES LESLIE	
ART UNIT	**PAPER NUMBER**
1641	

DATE MAILED: 10/14/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/771,680	ZHANG ET AL.	
	Examiner	Art Unit	
	James L. Grun	1641	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) 1-89 is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) 1-89 is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on 03 February 2004 is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date 2/22/05; 2/28/05.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

The search of the invention as instantly claimed in its entirety was not found burdensome by the examiner. However, applicant is reminded that a requirement for restriction can be made at any time before final action in the case at the discretion of the examiner.

The information disclosure statement filed 22 February 2005 fails to comply with the provisions of 37 CFR 1.97, 1.98 and MPEP § 609 because the submission was unsigned. It has been placed in the application file, but the information referred to therein has not been considered as to the merits. Applicant is advised that the date of any resubmission of any item of information contained in this information disclosure statement or the submission of any missing element(s) will be the date of submission for purposes of determining compliance with the requirements based on the time of filing the statement, including all requirements for statements under 37 CFR 1.97(e). See MPEP § 609 subsection III, C(1).

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefore, subject to the conditions and requirements of this title.

The following is a quotation of the first paragraph of 35 U.S.C. § 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

The specification is objected to under 35 U.S.C. § 112, first paragraph, as failing to provide an adequate written description of the invention, and failing to adequately teach how to make and/or use the invention, i.e. failing to provide an enabling disclosure.

Claims 1-47, 67-80, and 82-89 are rejected under 35 U.S.C. 101 because the claimed invention is not supported by either a specific, substantial, and credible asserted utility or a well-established utility.

With regard to "specific" utility, an application must disclose an asserted use for the invention as claimed which provides a well-defined and particular benefit to the public, a use particular to the claimed subject matter and not generally applicable to a broad class of invention, and which is not so vague as to be meaningless.

In order to satisfy the "substantial" utility requirement, an asserted use must show that the invention as claimed has a significant and presently available benefit to the public, a "real world" value.

The claims are directed to screening methods of determining conjugates and agents affecting their formation, isolated conjugates, and methods of treatment using isolated conjugates or agents identified in the screening.

Applicant urges that the isolated conjugates or agents could be used for therapy. As the intracellular function of the conjugates is not known (Malakhov et al., J. Biol. Chem. 278: 16608, 2003) and the extracellular conjugates have no known function and no diseases well-defined as associated therewith, and no guidance is provided in the specification for a currently available therapeutic use of the conjugates or agents, this is not seen as a substantial utility. Further unguided unpredictable experimentation would be required to define and refine a real world use for the conjugates or agents.

The screening methodology suggested in the instant application is disclosed as useful for the identification of target proteins conjugated to the interferon-stimulated gene of 15kDa (ISG15; ubiquitin cross-reactive protein) and the identification of candidate agents as to their potential future therapeutic function affecting conjugation and, thus, "characteristics" of the target protein. These are not specific or substantial asserted utilities. Inadequate guidance is presented for how to use the screening methodology because: the effects on the "characteristics" of the conjugated target protein, whether generically or specifically claimed, resulting from conjugation are not known and one would not know how to detect affects of agents on an unknown characteristic or exploit such changes for any treatment involving isolated conjugates. There is also nothing presented in the specification which would allow one to extrapolate from an in vitro conjugation assay system or treatment to the effect one would expect in situ (e.g. intracellularly) or in vivo. ISG15 conjugates lack an art accepted mode of action or a well established utility that would allow one to predict from an in vitro assay that any effect of any conjugate or agent determined in the screening assays would have an effect in vivo. For example, does the suggested assay correlate to another art accepted assay? Why would one skilled in the art accept the in vitro system as predictive or correlatable to the intended in vivo system? Mere identification of binding to a polypeptide does not equate to binding in a manner that modulates whatever in vivo pathway, if any, that the polypeptide affects, nor does it provide any insight as to how one uses such identification in a treatment. As taught in Malakhov et al. (J. Biol. Chem. 278: 16608, 2003), the biochemical function of ISG15-modification of target proteins remains unknown (see e.g. page 16613). It is entirely unknown and unpredictable if extracellular conjugates would have any therapeutic functions. It would therefore seem

unpredictable which compounds, if any, identified with the suggested methodology will be eventually shown to have any function, particularly any therapeutic function. The disclosure is based on speculation that any composition identified with the in vitro screening method would be effective in vivo. There is no currently available specific benefit seen in the asserted utility of gathering data regarding formation of conjugates of unknown function. Moreover, the in vivo success of any therapeutic composition is dependent not only upon a particular mode of action but also upon adequate concentrations of drug reaching the desired site of activity. Applicant provides no guidance which would allow one to predict the function of any conjugate or any identified agent, particularly extracellularly and/or in vivo. There are many pharmacokinetic properties of drugs such as half-life, deactivation by the liver, binding to plasma proteins, rapid excretion, etc. that would need to be determined and set forth to establish in vivo function. One would not know how to use the screening methods as disclosed because one would not be assured of the ability to use any conjugate or any agent identified in the screening assays as a therapeutic agent in the absence of further unpredictable undue experimentation to establish a nexus between the in vitro methods and in vivo function of any identified conjugate or agent. Utilities that require or constitute carrying out further unpredictable experimentation to identify or reasonably confirm a "real world" context of use are not substantial utilities.

Claims 1-47, 67-80, and 82-89 are rejected under 35 U.S.C. § 112, first paragraph. Specifically, since the claimed invention is not supported by either a specific, substantial, and credible asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention.

Claims 48-63 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention, and which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. Because, as set forth above, the intracellular function of particular conjugates is not known (see Malakhov et al.), the extracellular conjugates have no known function and no diseases well-defined as associated therewith, and no guidance is provided in the specification for a currently available diagnostic use of the conjugates, further unguided unpredictable experimentation would be required to define and refine appropriate patient populations or "malconditions" for a functional method for the diagnostic detection of the conjugates.

A patent is granted for a completed invention, not the general suggestion of an idea and how that idea might be developed into the claimed invention. In the decision of *Genentech Inc. v. Novo Nordisk*, 42 USPQ 2d 1001 (CAFC 1997), the court held that: "[p]atent protection is granted in return for an enabling disclosure of an invention, not for vague intimations of general ideas that may or may not be workable" and that "[t]ossing out the mere germ of an idea does not constitute enabling disclosure." The court further stated that: "when there is no disclosure of any specific starting material or of any of the conditions under which a process is to be carried out, undue experimentation is required; there is a failure to meet the enablement requirements that cannot be rectified by asserting that all the disclosure related to the process is within the skill

of the art", "[i]t is the specification, not the knowledge of one skilled in the art, that must supply the novel aspects of an invention in order to constitute adequate enablement."

Claims 64-66 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention, and which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The claims are drawn to a genus of antibodies of unknown structure and properties that bind to a genus of conjugates, only a few of which comprise known second target proteins, that are defined only by a first member of the conjugate to which the antibodies do not bind. In the absence of any guidance to antibodies which function as claimed, one would not know or be able to predict what structure or modifications were important and the amount of experimentation required to determine same would be undue. Note that even an enabling disclosure for the preparation and use of only a few analogs of a product does not enable all possible analogs where the characteristics of the analogs are unpredictable. Amgen Inc. v. Chugai Pharmaceutical Co. Ltd. (18 USPQ 2d 1027 (CAFC 1991)). Applicant is reminded that the written description provision of 35 USC 112 is severable from its enablement provision. In this regard, adequate written description requires more than a mere statement that a molecule is part of the invention and a reference to a potential method of isolating it. The compound itself is required. In *The Reagents of the University of California v. Eli Lilly* (43 USPQ2d 1398-1412), the court held that

a generic statement which defines a genus of molecules by only their functional activity does not provide an adequate written description of the genus. The court indicated that although applicants are not required to disclose every species encompassed by a genus, the description of a genus is achieved by the recitation of a representative number of molecules falling within the scope of the claimed genus. In the instant case, no members of the genus are described. Alternatively, to provide adequate written description and evidence of possession of a claimed genus, the specification must provide sufficient distinguishing identifying characteristics of the genus. The factors to be considered include disclosure of complete or partial structure, physical and/or chemical properties, functional characteristics when coupled with a known or disclosed structure/function correlation, or any combination thereof. In this case, the only factors present in the antibodies of the description and claims are a functional ability to bind conjugates of a known partial structure, but they are also not to bind the common known partial structure of the conjugate. There is no identification of any species of antibody or any particular portion of structure which must be preserved in the antigen or antibody. Accordingly, in the absence of sufficient recitation of distinguishing identifying characteristics of the antibodies or of the antigens, the specification does not provide adequate written description of the genus as claimed.

As set forth above, a patent is granted for a completed invention, not the general suggestion of an idea and how that idea might be developed into the claimed invention.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 21, 22, 24, and 84 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

In claim 21, "use" is not a valid method step.

In claim 22, "used" is not a valid method step.

In claim 24, "used" is not a valid method step.

Claim 84 is improper and unclear because it depends from itself.

The following is a quotation of the appropriate paragraphs of 35 U.S.C. § 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless --

(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-7, 10, 11, 13-22, 25-31, 34, 35, 37-53, 55, 56, 58-64, 83, 85-88 are rejected under 35 U.S.C. § 102(a) as being clearly anticipated by Hamerman et al. (J. Immunol. 168: 2415, March 2002).

Hamerman et al. teach methods and compositions meeting all of the limitations of the invention as instantly claimed. Conjugates were detected using Western blots and multiple antibodies binding thereto. Cells and animals were contacted with various agents and the effects on conjugate formation were determined.

Claims 1, 2, 7, 10, 11, 13, 14, 16, 19, 25, 26, 30, 31, 34, 35, 37-41, 43-49, 55, 56, 58, 60, 61, 63, 67-70, and 72-89 are rejected under 35 U.S.C. § 102(b) as being clearly anticipated by Johnson et al. (Biol. Reprod. 58: 898, 1998).

Johnson et al. teach methods and compositions meeting all of the limitations of the invention as instantly claimed. Conjugates were detected using Western blots and multiple antibodies binding thereto. Cells and animals were contacted with various agents and the effects on conjugate formation were determined, all proteins capable of being conjugated being detectable in the blots of the reference. Conjugates are taught to be secreted and thereby contact cells in culture and in patients.

Claims 1, 2, 7-11, 13, 14, 16, 19, 25, 26, 30-35, 37-47, 67-70, 72-76, 78, and 82-88 are rejected under 35 U.S.C. § 102(b) as being clearly anticipated by Loeb et al. (J. Biol. Chem. 267: 7806, 1992).

Loeb et al. teach methods and compositions meeting all of the limitations of the invention as instantly claimed. Conjugates were detected using Western blots and polyclonal antibodies binding thereto. Cells from humans were contacted with various agents and the effects on conjugate formation were determined, all proteins capable of being conjugated being detectable in the blots of the reference.

No claim is allowed.

The prior art made of record and not relied upon is considered pertinent to applicant's disclosure.

Malakhov et al. (J. Biol. Chem. 278: 16608, 2003) teach the screening assay as instantly disclosed. As taught in the reference, the biochemical function of ISG15-modification remains unknown (see e.g. page 16613).

Any inquiry concerning this communication or earlier communications from the examiner should be directed to James L. Grun, Ph.D., whose telephone number is (571) 272-0821. The examiner can normally be reached on weekdays from 9 a.m. to 5 p.m.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Long Le, SPE, can be contacted at (571) 272-0823.

The phone number for official facsimile transmitted communications to TC 1600, Group 1640, is (571) 273-8300.

Any inquiry of a general nature or relating to the status of this application, or requests to supply missing elements from Office communications, should be directed to the Group receptionist whose telephone number is (571) 272-1600.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

JLG

James L. Grun, Ph.D.
October 1, 2005

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10/03/05